Neoadjuvant Intraarterial Chemotherapy for Treatment of Malignant Vaginal Tumors in Children: A Single-Center Experience

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ABSTRACT

Six patients (aged 3–36 mo) with vaginal tumors (rhabdomyosarcoma and endodermal sinus tumor [EST]; n = 3 each) received intraarterial chemotherapy (IAC) and intravenous chemotherapy. Patients underwent internal iliac artery infusion with cisplatin, pirarubicin, and vindesine. Intravenous chemotherapy with vindesine, ifosfamide, and etoposide was administered after 3 weeks. Vaginal tumors disappeared in all patients after 2 or 3 cycles of alternating therapy. Two patients underwent resection of pelvic metastases. Intravenous consolidation chemotherapy was applied. Four patients were disease-free at a median follow-up of 5.8 years. One patient had pelvic recurrence treated with "salvage" therapy with IAC and surgery and was disease-free for 2.5 years.

ABBREVIATIONS

AFP = α-fetoprotein, EST = endodermal sinus tumor, IAC = intraarterial chemotherapy

Malignant tumors of the vagina in infants and children are extremely rare. Rhabdomyosarcoma and endodermal sinus tumor (EST) are the most common malignant tumors of the vagina in infants, and both are locally aggressive and capable of metastasis (1,2). The management of pediatric vaginal tumors has evolved from radical surgery to neoadjuvant chemotherapy followed by local control with surgery or radiation therapy (3,4).

Neoadjuvant intraarterial chemotherapy (IAC) has been reported to achieve favorable results in the treatment of locally advanced cervical cancer in adults (5–7). In the present retrospective observational study, we evaluate the feasibility and effect of neoadjuvant IAC combined with systemic chemotherapy for treatment of malignant vaginal tumors in children.

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None of the authors have identified a conflict of interest.

J Vasc Interv Radiol 2016; 27:996–1000

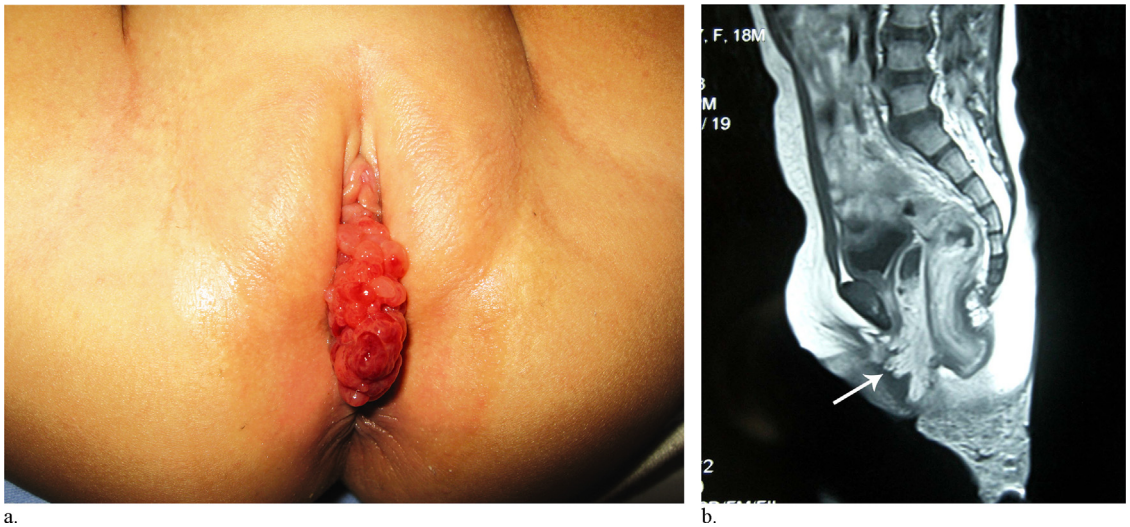
http://dx.doi.org/10.1016/j.jvir.2016.03.025

MATERIALS AND METHODS

From September 2002 to December 2013, six patients with malignant vaginal tumors were treated with neoadjuvant IAC and systemic chemotherapy at a single hospital. This study was approved by the institutional ethics committee, and informed consent was obtained from the children's parents before enrollment.

The median patient age at diagnosis was 1.27 years (range, 3–36 mo). All patients had the symptom of blood-tinged discharge from the vagina. Three patients had polypoid mass protruding from the vagina at admission. Contrast-enhanced magnetic resonance (MR) imaging, computed tomography (CT), and ultrasonography (US) showed a solitary mass in the vagina in each case (**Fig 1**). The tumor sizes ranged from 10 mm to 62 mm in maximum diameter (**Table**). Two patients presented with pelvic cavity tumor metastasis.

Biopsies were performed in all patients. Vaginoscopy was performed with the use of a pediatric cystoscope to visualize the vaginal tumor and obtain a biopsy specimen. The pathologic diagnosis was embryonal rhabdomyosarcoma of botryoid subtype in three cases and EST in three cases. All patients with EST had markedly elevated serum levels of α-fetoprotein (AFP; range, 916.9–10,446 μg/L). At the authors' institution, normal AFP levels in infants are 88 μg/L ± 87 at 3 months of age and 8.5 μg/L ± 5.5 at 8 months of age or more.



a. b.

Figure 1. Vaginal embryonal rhabdomyosarcoma of botryoid subtype in an 18-month-old girl. (**a**) A mass is seen protruding from the vagina. (**b**) Sagittal MR image shows a large tumor (arrows) in the vagina and protruding from the orificium vaginae.

The treatment consisted of alternating courses of IAC and systemic chemotherapy. IAC was performed under intravenous and caudal anesthesia. The femoral artery was catheterized via Seldinger technique with digital subtraction angiography guidance. A 5-F pigtail catheter (Cook, Bloomington, Indiana) was introduced into the abdominal aorta to perform aortography and iliac artery angiography. Tumor staining in the area of the vagina was visible (Fig 2a). A 4-F Cobra catheter (Cook) was placed in the anterior division of the internal iliac artery, with the tip of the catheter below the superior gluteal artery if possible (Fig 2b). The anticancer agents were then infused. The contralateral internal iliac artery intubation and drug infusion was performed via the same technique. The total amount of drugs infused was as follows: cisplatin 80 mg/m^2, pirarubicin 40 mg/m^2, and vindesine 3 mg/m^2. The drugs were mixed, diluted in 120–180 mL of normal saline solution, and injected by an external infusion pump over a period of 60 minutes. The procedure was performed bilaterally. The drug dose was divided depending on the predominant vascularization of the tumor. The drugs were infused with two thirds of the dose on the side of the predominant vascularization of the tumor and the remaining one third dose on the other side. To avoid ischemic necrosis of the viscera, no embolization agents were used. The catheter was removed after treatment. Intravenous hydration and alkalization were applied before, during, and after IAC. In addition, methylprednisolone and antiemetic agents were administered to prevent nausea and vomiting.

Intravenous chemotherapy was administered 3 weeks after IAC and consisted of vindesine 3 mg/m^2 on days 1 and 8 and ifosfamide 1,200 mg/m^2 and etoposide 100 mg/m^2 on days 2–4. Cycles of IAC and intravenous chemotherapy were repeated every 6 weeks. After two or three cycles of alternating IAC and intravenous chemotherapy, patients received four to six courses of intravenous chemotherapy as consolidation therapy. For the patients with rhabdomyosarcoma, two drug combinations were given at 3- or 4-week intervals: (*i*) alternating cycles of vindesine (3 mg/m^2 on days 1 and 8), carboplatin (300 mg/m^2 on day 2), and pirarubicin (20 mg/m^2 on days 3 and 4) and (*ii*) vindesine (3 mg/m^2 on days 1 and 8), ifosfamide (1,200 mg/m^2 on days 2–4), and etoposide (100 mg/m^2 on days 2–4). For the patients with EST, bleomycin (15 mg/m^2 on day 1), etoposide (100 mg/m^2 on days 1–3), and carboplatin (300 mg/m^2 on days 2 and 3) were given at 3- or 4-week intervals. The dosage of intraarterial and intravenous chemotherapy agents was reduced by 30% for patients with body weight of less than 10 kg.

During treatment, complete blood cell count and platelet count were repeated weekly; liver and kidney function tests, urinalysis, and toxicity evaluation were conducted before each treatment cycle. Toxicity was assessed according to World Health Organization criteria. MR imaging or CT scan, US, vaginoscopy and biopsy, chest radiography, and serum AFP measurement were repeated for every cycle of treatment to evaluate tumor response.

After treatment, all patients had regular follow-up visits at the outpatient department. Medical check-ups involved imaging examination of the pelvis, abdomen, and chest; complete hematologic analysis; renal and liver function tests; and serum AFP measurement.

RESULTS

There was no incidence of cardiologic toxicity, nephrotoxicity, hepatic dysfunction, or treatment-related death among all patients after IAC and intravenous chemotherapy. Grade II/III leukocytopenia occurred in three